ABSTRACT

A cell line (UISO-H-MEL-2) was established from the neoplastic cells of a patient with malignant melanoma during the natural course of the patient's treatment. The melanoma cells express defined MHC Class I histocompatibility determinants including determinants specified by the HLA-A2 Class I allele, along with a common melanoma-associated T-cell epitope derived from the tyrosinase gene. The gene for human interleukin-2 (IL-2) was transduced into the cells with a provirus (pZipNeoSVIL-2), packaged in GP+*env*AM12 cells. Integration of the IL-2 gene into genomic DNA of the transduced cells and its expression were established. The IL-2-secreting cell line (UISO-H-MEL-2-IL-2) was found to be free of recombinant retroviruses and other infectious agents. The IL-2-secreting cells will be subjected to 5000 rads X-irradiation and administered to 12 informed patients with metastatic malignant melanoma in a Phase I toxicity study. The dose of X-irradiation was sufficient to inactivate one hundred percent of the cells, but insufficient to completely inhibit IL-2 synthesis during a fourteen day period of analysis.

Patients who have failed all standard forms of treatment will become eligible for inclusion in the study if they develop metastatic melanoma, and if their tumor cells express products of the tyrosinase gene. The patients will differ with the cellular immunogen at no less than three of six MHC Class I alleles, but will share identity at the HLA-A2 Class I allele. The patient's antimelanoma immune response to the injected cells will be determined by both in vivo and in vitro parameters. Background studies performed in inbred mice indicate that X-irradiated IL-2-secreting cells that express both melanoma-associated antigens and allogeneic Class I histocompatability antigens are more antigenic in terms of their capacity to induce an antimelanoma response than X-irradiated IL-2-secreting melanoma cells. Of significance for the future potential of this form of therapy in melanoma patients, the period of survival of mice with established melanoma treated with the IL-2-secreting allogeneic cells was significantly ($P < 0.001$) longer than that of untreated animals, or animals treated with X-irradiated melanoma cells. An analogous protocol was reviewed and approved by the Recombinant DNA Advisory Committee of the National Institutes of Health.